



Clinical trial results:

A multicenter, Double-blind, RandOmised, two arm Parallel group trial to determine the effects of torasemide versus furosemide on one marker (PIP) of cardiac fibrosis in patient with Diastolic Heart Failure and diabetes mellitus type II

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2013-003601-25 |
| Trial protocol | DE |
| Global end of trial date | 20 September 2016 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 17 March 2022 |
| First version publication date | 17 March 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | DROP-PIP |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Charité - Universitätsmedizin Berlin |
| Sponsor organisation address | Augustenburger Platz 1, Berlin, Germany, Augustenburger Platz |
| Public contact | Prof. Dr. Carsten Tschöpe, Charité Universitätsmedizin Berlin, 49 30450 553712, Carsten.Tschoepe@charite.de |
| Scientific contact | Prof. Dr. Carsten Tschöpe, Charité Universitätsmedizin Berlin, 49 30450 553712, Carsten.Tschoepe@charite.de |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 20 September 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 September 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to determine whether torasemide is superior to furosemide in reducing one marker (PIP) of cardiac fibrosis in subjects with diastolic heart failure and diabetes type II.

Protection of trial subjects:

Qualified personnel monitored the trial, performed off- and on-site visits and assured scientific integrity. A control contact by phone after 44 days, a control visit after 5 months, a final visit for blinded PIP measurements, and secondary endpoint assessment after 9 months. For safety, we followed up the patients 2 weeks after the final visit.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 02 December 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects**Subjects enrolled per country**

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 35 |
| Worldwide total number of subjects | 35 |
| EEA total number of subjects | 35 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 35 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patient enrollment started 1 October 2014 and ended by 21 December 2015. Consecutive, eligible subjects meeting inclusion/exclusion criteria were considered for the study. The investigators verified that patients met all inclusion. Patients with PIP measurements ≥ 110 ng/mL or ≥ 70 ng/mL with LAVI .29 mL/m² at screening were eligible for randomis

Pre-assignment

Screening details:

A total of 214 patients were pre-screened, 51.4% declined to participate in DROP-PIP. Out of the 104 patients undergoing full screening, 14% had elevated PIP levels (≥ 110 ng/mL), and 54% of patients showed abnormal serum PIP levels in the grey zone of <110 ng/mL and ≥ 70 ng/mL.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Treatment (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Data analyst, Assessor |

Blinding implementation details:

Patients, the investigator team, individuals performing the assessments, and data analysts remained blinded to the identity of treatment until after database lock;

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Furosemide Group |

Arm description:

Patients were supplied with the drug at specified visits during the treatment period and received sufficient supply of the study drug to last until their next scheduled visit.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Furosemid |
| Investigational medicinal product code | Furosemid |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

furosemide 20 mg:

Patients were supplied with the drug at specified visits during the treatment period and received sufficient supply of the study drug to last until their next scheduled visit.

| | |
|------------------|-------------------|
| Arm title | Toraseamide Group |
|------------------|-------------------|

Arm description:

The investigators dispensed the study drug to the subject after the appropriate treatment allocated for the subject via randomisation and according to the protocol.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Toraseamid |
| Investigational medicinal product code | Toraseamid |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:**5mg Torasemide**

Patients were supplied with the drug at specified visits during the treatment period and received sufficient supply of the study drug to last until their next scheduled visit.

| Number of subjects in period 1 | Furosemide Group | Torasemide Group |
|---------------------------------------|------------------|------------------|
| Started | 18 | 17 |
| Completed | 16 | 12 |
| Not completed | 2 | 5 |
| Adverse event, serious fatal | 1 | - |
| Lost to follow-up | - | 1 |
| Protocol deviation | 1 | 4 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Furosemide Group |
|-----------------------|------------------|

Reporting group description:

Patients were supplied with the drug at specified visits during the treatment period and received sufficient supply of the study drug to last until their next scheduled visit.

| | |
|-----------------------|-----------------|
| Reporting group title | Torsemide Group |
|-----------------------|-----------------|

Reporting group description:

The investigators dispensed the study drug to the subject after the appropriate treatment allocated for the subject via randomisation and according to the protocol.

| Reporting group values | Furosemide Group | Torsemide Group | Total |
|-----------------------------|------------------|-----------------|-------|
| Number of subjects | 18 | 17 | 35 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults ≥18 years | 18 | 17 | 35 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 69.3 | 68.0 | |
| standard deviation | ± 8.1 | ± 8.3 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 11 | 4 | 15 |
| Male | 7 | 13 | 20 |
| Peripheral oedema | | | |
| Units: Subjects | | | |
| Peripheral oedema (yes) | 17 | 15 | 32 |
| Peripheral oedema (No) | 1 | 2 | 3 |
| Pulmonary congestions | | | |
| Units: Subjects | | | |
| Pulmonary congestions (yes) | 5 | 3 | 8 |
| Pulmonary congestions (no) | 13 | 14 | 27 |
| New York Heart Association | | | |
| NYHA | | | |
| Units: Subjects | | | |
| class I | 4 | 2 | 6 |
| class II | 6 | 10 | 16 |
| class III | 8 | 5 | 13 |
| Heart rate | | | |
| Units: b.p.m | | | |
| arithmetic mean | 74.8 | 72.3 | |
| standard deviation | ± 19.2 | ± 15.5 | - |
| Systolic BP | | | |
| Units: mmHg | | | |
| arithmetic mean | 136.8 | 130.2 | |
| standard deviation | ± 19.2 | ± 17.2 | - |
| Diastolic BP | | | |

| | | | |
|---|---------|---------|---|
| Units: mmHg | | | |
| arithmetic mean | 76.8 | 74.0 | |
| standard deviation | ± 9.9 | ± 12.3 | - |
| Body mass index | | | |
| Units: kg/m2 | | | |
| arithmetic mean | 34.8 | 34.5 | |
| standard deviation | ± 6.3 | ± 6.7 | - |
| Respiratory rate | | | |
| Units: /min | | | |
| arithmetic mean | 17.1 | 17.2 | |
| standard deviation | ± 1.8 | ± 1.4 | - |
| Cardiac structure and function LVEF | | | |
| left ventricular ejection fraction (LVEF) | | | |
| Units: LVEF (%) | | | |
| arithmetic mean | 62.5 | 61.0 | |
| standard deviation | ± 6.5 | ± 9.0 | - |
| Cardiac structure and function LVMI | | | |
| Left ventricular mass index LVMI | | | |
| Units: LVMI (g/m ²) | | | |
| arithmetic mean | 116.1 | 129.6 | |
| standard deviation | ± 26.6 | ± 27.3 | - |
| Cardiac structure and function LVEDVI | | | |
| left ventricular end diastolic ventricular volume index | | | |
| Units: LVEDVI (mL/m ²) | | | |
| arithmetic mean | 51.1 | 53.7 | |
| standard deviation | ± 14.0 | ± 18.4 | - |
| Cardiac structure and function LAVI | | | |
| left atrial volume index LAVI | | | |
| Units: LAVI (mL/m ²) | | | |
| arithmetic mean | 37.8 | 42.7 | |
| standard deviation | ± 8.9 | ± 14.4 | - |
| Cardiac structure and function E wave | | | |
| Units: m/s | | | |
| arithmetic mean | 79.6 | 87.5 | |
| standard deviation | ± 19.5 | ± 20.8 | - |
| Cardiac structure and function Deceleration time | | | |
| Units: time (ms) | | | |
| arithmetic mean | 231.4 | 235.5 | |
| standard deviation | ± 74.8 | ± 59.9 | - |
| Cardiac structure and function 6MWT | | | |
| 6-minute walk test | | | |
| Units: distance (m) | | | |
| arithmetic mean | 409.2 | 434.4 | |
| standard deviation | ± 110.2 | ± 127.6 | - |
| Laboratory PIP | | | |
| C-terminal propeptide of procollagen type I | | | |
| Units: ng/mL | | | |
| arithmetic mean | 133.1 | 99.7 | |
| standard deviation | ± 50.5 | ± 29.3 | - |
| Laboratory Sodium | | | |

| | | | |
|---|------------------|------------------|---|
| Units: mmol/L arithmetic mean standard deviation | 141.8 ± 2.9 | 141.1 ± 2.0 | - |
| Potassium Units: mmol/L arithmetic mean standard deviation | 4.4 ± 0.4 | 4.3 ± 0.5 | - |
| Laboratory Creatinine Units: mg/dL arithmetic mean standard deviation | 1.00 ± 0.3 | 1.0 ± 0.2 | - |
| Laboratory eGFR | | | |
| eGFR: estimated glomerular filtration using the Modification of Diet in Renal Disease formula | | | |
| Units: mL/min arithmetic mean standard deviation | 70.7 ± 18.7 | 73.5 ± 15.9 | - |
| Laboratory NT-proBNP | | | |
| NT-proBNP: N-terminal pro-B-type natriuretic peptide | | | |
| Units: pg/mL arithmetic mean standard deviation | 148.2 ± 141.4 | 201.8 ± 175.9 | - |
| Quality of life KCCQ total symptom | | | |
| Kansas City Cardiomyopathy Questionnaire | | | |
| Units: score arithmetic mean standard deviation | 62.7 ± 28.7 | 59.3 ± 26.6 | - |
| Quality of life KCCQ clinical summary | | | |
| Kansas City Cardiomyopathy Questionnaire | | | |
| Units: Score arithmetic mean standard deviation | 62.9 ± 31.3 | 58.1 ± 27.1 | - |
| Quality of life KCCQ overall summary | | | |
| Kansas City Cardiomyopathy Questionnaire | | | |
| Units: Score arithmetic mean standard deviation | 61.5 ± 28.3 | 56.6 ± 27.9 | - |

End points

End points reporting groups

| | |
|---|----------------------------|
| Reporting group title | Furosemide Group |
| Reporting group description: Patients were supplied with the drug at specified visits during the treatment period and received sufficient supply of the study drug to last until their next scheduled visit. | |
| Reporting group title | Toraseamide Group |
| Reporting group description: The investigators dispensed the study drug to the subject after the appropriate treatment allocated for the subject via randomisation and according to the protocol. | |
| Subject analysis set title | furosemide (PP) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Primary and secondary outcomes were analysed in the per-protocol population. | |
| Subject analysis set title | torasemide (PP) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Primary and secondary outcomes were analysed in the per-protocol population. | |
| Subject analysis set title | Diff (F-T) ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: difference between Furosemide and Torasemide | |
| Subject analysis set title | Diff (F-T) PP |
| Subject analysis set type | Per protocol |
| Subject analysis set description: difference between Furosemide and Torasemide in the per protocol group analysis | |
| Primary: Change of the PIP value PP | |
| End point title | Change of the PIP value PP |
| End point description: | |
| End point type | Primary |
| End point timeframe: 9 months | |

| End point values | furosemide (PP) | torasemide (PP) | Diff (F-T) PP | |
|--------------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 16 | 12 | 28 | |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | | | | |
| Percentage PIP change | 3.08 (± 29.30) | 3.72 (± 28.17) | -064 (± 28.83) | |
| Absolute PIP change | 1.15 (± 38.11) | -1.25 (± 29.10) | 2.40 (± 34.59) | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | change of the percentage in PIP values in PP |
| Comparison groups | furosemide (PP) v torasemide (PP) |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 2-sided |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.27 |
| upper limit | 21.99 |

| | |
|---|--|
| Statistical analysis title | change of the absolute values of PIP in PP |
| Comparison groups | torasemide (PP) v furosemide (PP) |
| Number of subjects included in analysis | 28 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 2-sided |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -24.75 |
| upper limit | 29.55 |

Secondary: Change of the Cardiac structure and function LVMI

| | |
|---|---|
| End point title | Change of the Cardiac structure and function LVMI |
| End point description: LVMI, left ventricular mass index | |
| End point type | Secondary |
| End point timeframe: 9 months | |

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|------------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: g/m ² | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| LVMI (g/m ²) | -24.065546 (-83.80 to 30.20) | -8.930035 (-50.00 to 23.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change of the Cardiac structure and function LVEDVI and LAVI

| | |
|------------------------|--|
| End point title | Change of the Cardiac structure and function LVEDVI and LAVI |
| End point description: | LAVI, left atrial volume index; LVEDVI, left ventricular end-diastolic volume index; |
| End point type | Secondary |
| End point timeframe: | 9 months |

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|-----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: mL/m ² | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| LVEDVI | -1.369978 (-32.80 to 11.00) | 8.974017 (-15.00 to 100.00) | | |
| LAVI | 11.845524 (-22.00 to 28.00) | -4.433040 (-25.80 to 17.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change of the Cardiac structure and function E-wave

| | |
|------------------------|---|
| End point title | Change of the Cardiac structure and function E-wave |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | 9 months |

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: m/s | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| E wave | 3.227311 (-19.20 to 43.00) | -0.925811 (-33.00 to 22.40) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change of the Cardiac structure and function Deceleration

| | |
|------------------------|---|
| End point title | Change of the Cardiac structure and function Deceleration |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 9 months | |

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|-----------------------------|----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: time in ms | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| Deceleration time | -0.149871 (-12.00 to 10.00) | -4.746263 (-29.00 to 7.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change of the Cardiac structure and function in 6MWT

| | |
|------------------------|--|
| End point title | Change of the Cardiac structure and function in 6MWT |
| End point description: | |
| End point type | Secondary |

End point timeframe:

9 months

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|------------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: distance in m | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| 6MWT distance | -24.065546 (-83.80 to 30.20) | -8.930035 (-50.00 to 23.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory change in Sodium and Potassium

| | |
|------------------------|---|
| End point title | Laboratory change in Sodium and Potassium |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 9 months | |

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|--------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: mmol/L | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| Sodium | 0.848150 (-5.00 to 4.00) | 1.051091 (-3.00 to 5.00) | | |
| Potassium | 0.146975 (-0.50 to 1.10) | -0.103028 (-1.00 to 0.50) | | |

| | |
|----------------------------|--|
| Attachments (see zip file) | Graphical display of safety parameters/Figure S1 Graphical |
|----------------------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory Change in Creatinine

| | |
|-----------------|---------------------------------|
| End point title | Laboratory Change in Creatinine |
|-----------------|---------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

9months

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|--------------------------|--------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: mg/dL | | | | |
| arithmetic mean (full range (min-max)) | 0.051509 (-0.26 to 0.60) | 0.002024 (-0.32 to 0.38) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Laboratory Change in NTproBNP

| | |
|-----------------|-------------------------------|
| End point title | Laboratory Change in NTproBNP |
|-----------------|-------------------------------|

End point description:

NT-proBNP, N-terminal pro-B-type natriuretic peptide

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

9 months

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|-------------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: pg/mL | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| NT-proBNP | 100.427856 (-64.60 to 696.50) | 19.663125 (-115.50 to 476.30) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Quality of life (KCCQ)

| | |
|-----------------|----------------------------------|
| End point title | Change in Quality of life (KCCQ) |
|-----------------|----------------------------------|

End point description:

Kansas City Cardiomyopathy Questionnaire

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

9 months

| End point values | furosemide (PP) | torasemide (PP) | | |
|--|----------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 12 | | |
| Units: Score | | | | |
| arithmetic mean (full range (min-max)) | | | | |
| KCCQ total symptom | 1.844597 (-25.00 to 41.67) | 2.262459 (-25.00 to 33.33) | | |
| KCCQ clinical summary | 1.168577 (-19.79 to 36.77) | 3.951155 (-15.63 to 31.25) | | |
| KCCQ overall summary | 3.560723 (-16.93 to 27.08) | -0.038717 (-18.75 to 27.08) | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Difference between Furosemide and Torasemide in ITT Group

| | |
|-----------------|---|
| End point title | Difference between Furosemide and Torasemide in ITT Group |
|-----------------|---|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

9 months

| End point values | Diff (F-T) ITT | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 35 | | | |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | | | | |
| Percentage PIP change | 0.11 (± 25.63) | | | |
| Absolute PIP change | 1.90 (± 30.70) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

9 months

Adverse event reporting additional description:

One non-cardiac death with no relation to the study drug or procedures was observed in the furosemide group. Overall, 17.1% of patients dropped out due to other causes, mainly refractory congestion requiring intensified therapy outside of the protocol

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|-----|
| Dictionary name | own |
|-----------------|-----|

| | |
|--------------------|---|
| Dictionary version | 1 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Furosemide |
|-----------------------|------------|

Reporting group description: -

| | |
|-----------------------|-------------|
| Reporting group title | Toraseamide |
|-----------------------|-------------|

Reporting group description: -

| Serious adverse events | Furosemide | Toraseamide | |
|--|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 18 (61.11%) | 11 / 17 (64.71%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Investigations | | | |
| fracture, surgery, depression, pulmonary infection | | | |
| subjects affected / exposed | 5 / 18 (27.78%) | 4 / 17 (23.53%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| refractory congestion, cardiac decompensation | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 17 (11.76%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| acute coronary syndrome, atrial flutter/fibrillation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 3 / 18 (16.67%) | 3 / 17 (17.65%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 17 (5.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| anuresis, acute renal failure | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 17 (5.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Furosemide | Torsemide | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 15 / 18 (83.33%) | 10 / 17 (58.82%) | |
| Investigations | | | |
| Hyperkalaemia (>5.2 mmol/L) | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 17 (17.65%) | |
| occurrences (all) | 1 | 3 | |
| Hypotension (≤100 mmHg systolic blood pressure) | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 17 (11.76%) | |
| occurrences (all) | 1 | 2 | |
| Injury, poisoning and procedural complications | | | |
| Falls | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 17 (5.88%) | |
| occurrences (all) | 2 | 1 | |
| Gastrointestinal disorders | | | |
| Refractory congestion | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 17 (5.88%) | |
| occurrences (all) | 2 | 1 | |
| Renal and urinary disorders | | | |

| | | | |
|--|----------------------------|----------------------|--|
| Worsening renal function 0.3mg/dL increase in Creatinine) subjects affected / exposed occurrences (all) | (> 9 / 18 (50.00%) 9 | 3 / 17 (17.65%) 3 | |
|--|----------------------------|----------------------|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 08 April 2014 | #1 Amendment: Update protocol V1.3. from 2013/08/07 Modul 1 |
| 02 March 2015 | #2 Amendment: Update study protocol + Synopse V1.3 |
| 24 August 2015 | #3 Amendment: Update study protocol V1.4 from 2015/ 08/06, update Modul 1 |
| 05 April 2016 | #4 Amendment: Change manufacturer of study medication., update Modul 1 - IMPD, SmPC |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28891228>